REMARKS

I. Status of the Application

This paper responds to a final Office Action, which was mailed on January 7, 2004. The original application was filed with claims 1-17. In a response to a telephonic restriction requirement, Applicant elected to pursue Group I invention (claims 1-9) and gabapentin species. A non-final Office action mailed on September 13, 2001 rejected claims 1-9 and withdrew from consideration claims 10-17 as being drawn to a non-elected invention. Applicant filed a response to the non-final Office action on February 12, 2002, amending claims 1-9 and adding new claims 18-22. A subsequent final Office action mailed on May 30, 2002, rejected claims 1-9 and 18-22. Applicant filed an after-final amendment on July 30, 2002, which was not entered. Applicant subsequently filed a Request for Continued Examination (RCE), which amended claim 1 and added new clams 23 and 24. A non-final Office action was mailed on April 10, 2003, which rejected claims 1-9 and 18-22. Applicant filed a response on September 10, 2003, which amended claims 1, 9, 18, 20, and 24, and canceled claims 10-17 without prejudice or disclaimer.

The present paper requests cancellation of claims 1-9 and 18-24 without prejudice or disclaimer and requests entry of new claims 25-31. Applicant submits that entry of this after final amendment is proper because it raises no new issues requiring a further search of the prior art and it places the claims in condition for allowance. Applicant respectfully requests consideration of claims 25-31 in view of the above amendment and the following remarks. By the action taken here, Applicant in no way intends to surrender any range of equivalents beyond that needed to patentably distinguish the claimed invention as a whole over the prior art. Applicant expressly reserves all such equivalents that may fall in the range between Applicant's literal claim recitations and combinations taught or suggested by the prior art.

II. New Claims 25-32

New claim 25 includes the limitations of previously amended claim 9, but also requires that the claimed composition be a "pharmaceutical dosage form." Support for this limitation can be found throughout the specification, including page 1, lines 14-19 and page 13, lines 11-16. New claims 26-31, which depend on claim 25, include the limitations of previously amended

claims 2-5, 7, and 18, respectively. New dependent claim 32 adds that the 4-amino-3-substituted-butanoic acid derivative be pregabalin. Applicant submits that none of the amendments introduce new matter.

III. Rejection of Claims 18 and 20 Under 35 U.S.C. § 102

The final Office action rejected claims 18 and 20 under 35 U.S.C. § 102(b) as allegedly being anticipated by Woodruff (US 5,084,479) because it "discloses a solution comprising N-methyl-D-aspartic acid and gabapentin (column 8, line 5)." As noted above in section II of this paper, Applicant has added claim 25, which requires that the claimed composition be a "pharmaceutical dosage form." Since none of the solutions containing N-methyl-D-aspartic acid are pharmaceutical dosage forms, Woodruff cannot anticipate claims 25-32. Applicant respectfully requests withdrawal of this rejection as it applies to claims 25-32.

Furthermore, Woodruff cannot be used to render claims 25-32 obvious because it teaches away from any pharmaceutical dosage form that includes N-methyl-D-aspartic acid (NMDA), gabapentin, and an auxiliary agent. In Woodruff, solutions of gabapentin and NMDA were apparently used to show that gabapentin reduces depolarization of paraventricular thalamus neurons due to NMDA (column 8, lines 20-49). As described in Woodruff, "these results indicate that gabapentin has additional therapeutic indications . . . [since] over stimulation of NMDA receptors has been implicated in the etiology of neuronal damage induced by anoxia, stroke, hypoglycemia, Huntington's disease, as well as epilepsy" (column 3, lines 9-14). Since Woodruff teaches that gabapentin counteracts the effects of NMDA, and over stimulation of NMDA receptors has been implicated in neuronal damage, adding NMDA to a pharmaceutical preparation containing gabapentin would run counter to Woodruff's teachings. Applicant therefore submits that all of the claims of the present application are patentable over Woodruff.

IV. Rejection of Claims 1-9, 19, 21-24 Under 35 U.S.C. § 103

The final Office action rejected claims 1-9, 19, and 21-24 under 35 U.S.C. § 103(a) as allegedly being unpatentable over Seiler et al. (Gen. Pharmac. Vol. 15, No. 4. pp 367-69, 1984) in view of Costa et al. (US 5,248,678).

Applicant respectfully submits that the rejection, as applied to new claims 25-32, is improper because it does not establish a prima facie case of obviousness. To establish a prima facie case of obviousness, there must be (1) some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings; there must be (2) a reasonable expectation of success; and (3) the reference (or references when combined) must teach or suggest all the claim limitations. See, MPEP § 2143.01 (Feb. 2003). Applicant respectfully submits that there is no suggestion or motivation to combine Seiler et al. and Costa et al.

As an initial matter, Applicant reiterates that Costa et al. cannot be combined with Seiler et al. because the latter reference teaches away from the combination. According to the Office action, "Seiler et al. teaches or suggests the synergistic anticonvulsant effects of a GABA agonist and alpha-amino acid such as glycine. The reference discloses muscimol as the specific example of a GABA agonist." Seiler et al, however, warns against administering muscimol and glycine together so as "to avoid the potential inhibition of muscimol absorption by glycine" (page 367, Methods section). Thus, not only does Seiler et al. fail to teach or suggest combining gabapentin and an α amino acid, it teaches away from making a pharmaceutical preparation comprised of gabapentin and an α amino acid.

The final Office action contends that Seiler et al. only refers to "subcutaneous administration," but nothing in Seiler et al. indicates that the inhibition of muscimol absorption by glycine would not occur with other administration routes. Even if Seiler et al. were limited to subcutaneous administration, Applicant disclosed that the claimed pharmaceutical composition could be dosed through subcutaneous administration, i.e., via injection. See, e.g., page 1, lines 14-19 and page 13, lines 11-12. The final Office action also contends that other references (US 4,595,697 to Seiler et al., US 4,595,697 to Seiler et al., Liu et al., European Journal of Pharmacology 182:109-115 (1990), and Peterson et al., Neuropharmacology 29(4):399-409 (1990)) teach or suggest the "pharmaceutical preparation comprising GABA agonist and glycine." However, despite the disclosure of pharmaceutical compositions in the two patents to Seiler et al., it appears that none of these latter references provide examples that show administration of a GABA agonist and an α amino acid at the same time. Furthermore, Peterson

et al. indicates that the potency and selectivity of a number of anticonvulsants are unaffected by glycine.

In addition, the final Office action's contention that the references teach or suggest a "pharmaceutical preparation comprising GABA agonist and glycine" represents an impermissible "obvious to try" rationale. GABA agonists potentially embrace a large number of compounds. Indeed, Costa et al. lists a number of compounds purported to be GABA agonists, but besides muscimol, none of the cited references indicate that glycine may improve the compounds' anticonvulsive properties. Moreover, Peterson et al. indicates that the potency and selectivity of a number of anticonvulsants—including sodium divalproate (valproic acid) which is listed in Costa et al.—are unaffected by glycine. Thus, far from teaching a "pharmaceutical preparation comprising GABA agonist and glycine," the cited references teach that glycine improves the anticonvulsive properties of a few GABA agonists, namely, muscimol and γ vinyl GABA, which is insufficient to support an obviousness rejection.

VI. Conclusion

In view of the foregoing, Applicant respectfully submits that all pending claims are patentable over the prior art of record. If the Examiner has any questions, Applicant requests that the Examiner telephone the undersigned.

Applicant believes that no fees are required to file the present amendment. However, if any fees required in connection with the filing of this paper, please charge deposit account number 23-0455.

Respectfully submitted,

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